

| | | |
|---|------------|---------|
| => FIL MEDLINE, BIOSIS, CA, CAPLUS, CAOLD, EMBASE, USPATFULL, PROMT | | |
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 0.32 | 17.01 |

FILE 'MEDLINE' ENTERED AT 00:57:17 ON 11 FEB 2002

FILE 'BIOSIS' ENTERED AT 00:57:17 ON 11 FEB 2002
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FILE 'USPATFULL' ENTERED AT 00:57:17 ON 11 FEB 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'PROMT' ENTERED AT 00:57:17 ON 11 FEB 2002
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=> s l2
L3 11 L2

=> s sericin or silkworm gene or sericinase
L4 2746 SERICIN OR SILKWORM GENE OR SERICINASE

=> s l3 or l4
L5 2746 L3 OR L4

=> s skin cancer
L6 25029 SKIN CANCER

=> s l5 and l6
L7 5 L5 AND L6

=> dup rem
ENTER L# LIST OR (END):l7
DUPLICATE IS NOT AVAILABLE IN 'CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L7
L8 5 DUP REM L7 (0 DUPLICATES REMOVED)

=> d l8 1-5 bib, ab, kwic

L8 ANSWER 1 OF 5 PROMT COPYRIGHT 2002 Gale Group

AN 2001:128352 PROMT
TI R&D in the New Cosmetic Age.
AU Mufti, Jabbar; Macchio, Ralph
SO Household & Personal Products Industry, (Jan 2001) Vol. 38, No. 1, pp.
56.
ISSN: 0090-8878.
PB Rodman Publications, Inc.
DT Newsletter
LA English
WC 5492

FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Novel raw materials are helping to drive researchers to develop
high-tech cosmetics that perform a variety of functions.
THIS IS THE FULL TEXT: COPYRIGHT 2001 Rodman Publications, Inc.

Subscription: \$48.00 per year. Published monthly. 17 S. Franklin
Turnpike,
Box 555, Ramsey, NJ 07446.

TX Carbohydrates . . . similar to animal-derived collagen. Therefore,
it

is a genuine replacement for the animal-derived collagen. Another example
of glycoprotein has been **sericin**, which was isolated from
silk.[11] A new lip therapy ingredient, palmitoyl oligopeptide, recorded
excellent results moisturizing and fullness subjective testing.[12]

Wine . . . the leaves of the ericaceae and rosaceae, are used in
cosmetics as a natural whitening agent. Soy isoflavonose may fight
skin cancer, according to studies. Grape seed extract
containing flavonoids (PCAs), an anti-oxidant, is comparable to soy
extract containing isoflavones. The biggest. . .

L8 ANSWER 2 OF 5 CA COPYRIGHT 2002 ACS

AN 136:31673 CA

TI **Sericin skin cancer** preventive agent

IN Jin, Zongxuan; Muramatsu, Koichiro; Yamada, Hideyuki; Fuwa, Naozumi;
Hibasami, Hiroshige

PA Kabushiki Kaisha Aioi Hakko, Japan; Seiren Kabushiki Kaisha

SO U.S. Pat. Appl. Publ., 4 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|----------|
| PI | US 2001053759 | A1 | 20011220 | US 2001-863316 | 20010524 |
| | JP 2001354584 | A2 | 20011225 | JP 2000-178776 | 20000614 |
| | EP 1166795 | A2 | 20020102 | EP 2001-113730 | 20010605 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRAI | JP 2000-178776 | A | 20000614 | | |

AB The present invention provides a **skin cancer**
preventive agent that inhibits the promotion of carcinogenesis of
skin cancer while having high levels of safety and
stability as well as being free of adverse side effects. The present
invention is characterized by contg. **sericin**.

TI **Sericin skin cancer** preventive agent

AB The present invention provides a **skin cancer**
preventive agent that inhibits the promotion of carcinogenesis of
skin cancer while having high levels of safety and
stability as well as being free of adverse side effects. The present
invention is characterized by contg. **sericin**.

ST **sericin skin cancer prevention**
IT Sericins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(**sericin skin cancer** preventive agent)
IT Antitumor agents
(skin carcinoma; **sericin skin cancer**
preventive agent)
IT Antitumor agents
(skin; **sericin skin cancer** preventive
agent)

L8 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2001:924315 CAPLUS
DN 136:31673
TI **Sericin skin cancer** preventive agent
IN Jin, Zongxuan; Muramatsu, Koichiro; Yamada, Hideyuki; Fuwa, Naozumi;
Hibasami, Hiroshige
PA Kabushiki Kaisha Aioi Hakko, Japan; Seiren Kabushiki Kaisha
SO U.S. Pat. Appl. Publ., 4 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

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| | JP 2001354584 | A2 | 20011225 | JP 2000-178776 | 20000614 |
| | EP 1166795 | A2 | 20020102 | EP 2001-113730 | 20010605 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRAI | JP 2000-178776 | A | 20000614 | | |

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preventive agent that inhibits the promotion of carcinogenesis of
skin cancer while having high levels of safety and
stability as well as being free of adverse side effects. The present
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TI **Sericin skin cancer** preventive agent
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preventive agent that inhibits the promotion of carcinogenesis of
skin cancer while having high levels of safety and
stability as well as being free of adverse side effects. The present
invention is characterized by contg. **sericin**.
ST **sericin skin cancer** prevention
IT Sericins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(**sericin skin cancer** preventive agent)
IT Antitumor agents
(skin carcinoma; **sericin skin cancer**
preventive agent)
IT Antitumor agents
(skin; **sericin skin cancer** preventive
agent)

L8 ANSWER 4 OF 5 USPATFULL
AN 2001:233530 USPATFULL
TI **Skin cancer** preventive agent
IN Jin, Zongxuan, Nishio, China
Muramatsu, Koichiro, Nishio, Japan

Yamada, Hideyuki, Fukui, Japan
Fuwa, Naozumi, Fukui, Japan
Hibasami, Hiroshige, Mie, Japan

PA KABUSHIKI KAISHA AIOI HAKKO & SEIREN KABUSHIKI KAISHA (non-U.S. corporation)

PI US 2001053759 A1 20011220

AI US 2001-863316 A1 20010524 (9)

PRAI JP 2000-178776 20000614

DT Utility

FS APPLICATION

LREP ARENT FOX KINTNER, POLTKIN & KAHN, PLLC, Suite 600, 1050 Connecticut Avenue, N.W., Washington, DC, 20036-5339

CLMN Number of Claims: 3

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 220

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a **skin cancer** preventive agent that inhibits the promotion of carcinogenesis of **skin cancer** while having high levels of safety and stability as well as being free of adverse side effects. The present invention is characterized by containing **sericin**.

TI **Skin cancer** preventive agent

AB The present invention provides a **skin cancer** preventive agent that inhibits the promotion of carcinogenesis of **skin cancer** while having high levels of safety and stability as well as being free of adverse side effects. The present invention is characterized by containing **sericin**.

SUMM [0002] The present invention relates to a **skin cancer** preventive agent that uses natural **sericin** for its raw material, has high safety and stability, is free of adverse side effects, and can be used in. . .

SUMM [0006] In consideration of the above requirements, the object of the present invention is to provide a **skin cancer** preventive agent that has high levels of safety and stability while being free of adverse side effects.

SUMM [0007] As a result of focusing on the naturally-occurring cocoon protein, **sericin**, the inventors of the present invention found that **sericin** exhibits an inhibitory action on promotion of skin carcinogenesis at low concentrations, thereby leading to completion of the present invention. Namely, the invention of claim 1 relates to a **skin cancer** preventive agent that contains **sericin**.

SUMM [0008] The invention of claim 2 relates to the **skin cancer** preventive agent according to claim 1 wherein, the **sericin** is a hydrolysis product of **sericin**.

SUMM [0009] In addition, the invention of claim 3 relates to the **skin cancer** preventive agent according to either of claims 1 or 2 wherein, the weight average molecular weight of **sericin** is from 5,000 to 100,000.

DETD [0011] The present invention is a naturally-occurring preventive agent for **skin cancer** having **sericin** (including hydrolysis products of **sericin**) for its active ingredient. The **sericin** used in the present invention is normally extracted by solvent or physically separated from the cocoon or raw silk expelled.

DETD [0013] Examples of extraction solvents for obtaining **sericin** from the above materials include cold water, hot water, water-containing

alcohol and other hydrophilic solvents. For example, after boiling domesticated. . .

DETD [0014] Moreover, **sericin** having a weight average molecular weight from 5,000 to 100,000 and a particularly superior inhibitory action on promotion of skin. . . average molecular weight exceeds 100,000, mixing with other suitably used drugs such as carriers, fillers and diluents becomes poor. Consequently, **sericin** (and including hydrolysis products of **sericin**) having a weight average molecular weight from 5,000 to 100,000 are used preferably.

DETD [0016] Although the **sericin** having superior inhibitory action on promotion of skin carcinogenesis obtained in this manner has a high molecular weight, it is. . .

DETD [0018] Since **sericin** is a naturally-occurring substance, it is highly safe, and can be added to drugs, over-the-counter drugs, cosmetics, foods and health. . .

DETD . . . filtration chromatography to obtain a fraction having a molecular weight from 10,000 to 50,000 followed by freeze-drying to obtain solid **sericin** having a weight average molecular weight of 30,000. Moreover, a solution in which this solid **sericin** was dissolved in distilled water to a concentration of 2.5% (first example of the present invention) and a solution in which this solid **sericin** was dissolved in distilled water to a concentration of 5% (second example of the present invention) were additionally obtained.

DETD [0021] The following experiment was conducted to investigate the inhibitory action on promotion of skin carcinogenesis using the **sericin** solutions of the above first and second examples obtained in the manner described above.

DETD . . . applied at the same site on the skin of the mice three times a week for 20 weeks to induce **skin cancer** in the mice. (Control group) In parallel with the above experiment using the control group, DMBA and TPA were applied in. . . the control group to

the mice of test groups A and B, and for each application of TPA, the 2.5% **sericin** solution of the first example was applied to the skin of the mice of test group A, while the 5% **sericin** solution of the second example was applied to the skin of the mice of test group B, after each application. . . of 100 82 1 of each solution was applied three times a week for 20 weeks. The total amount of **sericin** applied was 2.5 mg in the mice of test group A, and 5 mg in the mice of test group. . .

DETD [0024] The time-dependent inhibitory action on skin carcinogenesis in mice by the present invention (**sericin**) with respect to promotion of skin carcinogenesis was investigated for the above test group A as compared with the control group. The carcinogenesis inhibition rate of mouse **skin cancer** was determined by determining the number of papilloma having a diameter of 2 mm or more that formed on the. . . control group to which only acetone solutions of DMBA and TPA were applied, in test group A to which the **sericin** of the first example was applied, initial papilloma did not occur until week 14. In addition, as a result of. . . found to be inhibited by 80% in test group A as compared with the control group. In this manner, the **skin cancer** preventive agent of the first example was clearly determined to exhibit preventive effects on the occurrence of papilloma on mice. . .

DETD . . . groups of the above first and second examples in week 20 in

order to investigate the concentration-dependent inhibitory action of **sericin** on the number of papilloma on mice skin, the number of papilloma was lower in test group B, in which. . . 100% was demonstrated in test group B. On the basis of these findings, it was determined that the larger the **sericin** concentration (applied amount), the greater the preventive effect on the occurrence of mouse skin papilloma.

DETD [0026] On the basis of these results, it was clearly determined that application of the **skin cancer** preventive agent of the present invention makes it possible to confirm that the promotion of

carcinogenesis of mouse skin can be inhibited, and that the **skin cancer** preventive agent of the present invention has a function that prevents the occurrence of **skin cancer**.

DETD [0027] As has been explained above, according to the **skin cancer** preventive agent of the present invention, the use of **sericin** makes it possible to inhibit the occurrence of **skin cancer** with high levels of safety and stability without the occurrence of adverse side effects, while also allowing long-term use.

DETD [0028] In addition, the **skin cancer** preventive agent of the present invention can be used as a functional ingredient that prevents **skin cancer** in a wide range of fields, including drugs, skin external preparations, over-the-counter drugs, cosmetics and lotions.

CLM What is claimed is:

1. A **skin cancer** preventive agent containing **sericin**.
2. The **skin cancer** preventive agent according to claim 1 wherein, the **sericin** is a hydrolysis product of **sericin**.
3. The **skin cancer** preventive agent according to either of claims 1 or 2 wherein, the weight average molecular weight of **sericin** is from 5,000 to 100,000.

L8 ANSWER 5 OF 5 USPATFULL
AN 2001:32816 USPATFULL
TI Composition for external use
IN Abe, Koji, Kanagawa, Japan
Miyahara, Reiji, Kanagawa, Japan
Nanba, Tomiyuki, Kanagawa, Japan
Nakamura, Tadashi, Kanagawa, Japan
Hayashi, Toshikatsu, Kanagawa, Japan
Seki, Nozomiko, Kanagawa, Japan
Uehara, Keiichi, Osaka, Japan
Nishiyama, Syoji, Kanagawa, Japan
PA Shiseido Company, Ltd., Tokyo, Japan (non-U.S. corporation)
PI US 6197318 B1 20010306
WO 9926590 19990603
AI US 1999-341146 19990716 (9)
WO 1998-JP4040 19980909
19990716 PCT 371 date
19990716 PCT 102(e) date
PRAI JP 1997-337916 19971120
DT Utility
FS Granted
EXNAM Primary Examiner: Dodson, Shelley A.

LREP Townsend & Banta
 CLMN Number of Claims: 27
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 2291

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A composition for external use which contains xyloglucan. It preferably further contains an ultraviolet shielding agent, a thickening polysaccharide, a thickening polysaccharide and **sericin**, a carboxyvinylpolymer, or an alkyl-modified carboxyvinylpolymer.

AB . . . external use which contains xyloglucan. It preferably further contains an ultraviolet shielding agent, a thickening polysaccharide, a thickening polysaccharide and **sericin**, a carboxyvinylpolymer, or an alkyl-modified carboxyvinylpolymer.

SUMM . . . generation of age spots or freckles and skin aging, as well as to prevent generation of skin diseases such as **skin cancer**. When an external-use composition is processed into an emulsion such as milky lotion or cream or is stabilized, a surfactant.

SUMM C. A third mode of the present invention is directed to an external-use composition in which xyloglucan, thickening polysaccharides, and **sericin** are incorporated (hereinafter the composition will be referred to as the "external-use composition of the third mode of the present. . .

SUMM The present inventors found that the aforementioned external-use composition containing xyloglucan, thickening polysaccharides, and **sericin** has not only good moisturizing effect on the skin but also favorable sensation in use, such as good fit for. . .

SUMM **Sericin** which may be incorporated into the composition is a hydrophilic protein contained in silk threads which are produced by a.

SUMM In the external-use composition of the third mode of the present invention, the amount of incorporated **sericin** is 0.001-5.0 wt. %, preferably 0.01-3.0 wt. %, with respect to the entirety of the composition.

SUMM In the external-use composition of the third mode of the present invention, when **sericin** is incorporated in an amount of less than 0.001 wt. % with respect to the entirety of the composition, substantial. . . no stickiness. When the amount thereof is more than 5.0 wt. % with respect to the entirety of the composition, **sericin** forms a film on the skin and provides a sticky sensation.

SUMM In addition to the aforementioned ingredients (xyloglucan, thickening polysaccharides, **sericin**), other ingredients which are usually utilized for external-use compositions may be appropriately incorporated

into the external-use composition of the third. . .

SUMM . . . gamma.-oryzanol, allantoin, glycyrrhizic acid (salts), glycyrrhetic acid and derivatives thereof, extracts from a variety of animals and plants (other than **sericin**), hinokitiol, bisabolol, eucalyptus, thymol, inositol, saponins, pantothenyl ethyl ether, ethynylestradiol, tranexamic acid, arbutin, cepharanthine, and placenta extract.

DETD . . . -- --

(5) hydroxyethylcellulose -- -- -- 2.0 -- --

(6) xanthan gum -- -- -- 2.0 --

(7) **sericin** -- -- -- 2.0

(8) preservative s.a. s.a. s.a. s.a. s.a. s.a.

(9) perfume s.a. s.a. s.a. s.a. . .

DETD . . . 2.0 2.0 0.1 2.0 0.1

| | | | | | | |
|---------------------------|------|------|------|------|------|------|
| (4) hydroxyethylcellulose | 1.0 | 1.0 | 0.1 | 2.0 | -- | 0.1 |
| (5) xanthan gum | 1.0 | 1.0 | -- | -- | 0.1 | 0.1 |
| (6) sericin | 1.0 | 0.1 | 1.0 | 1.0 | 1.0 | 1.0 |
| (7) preservative | s.a. | s.a. | s.a. | s.a. | s.a. | s.a. |
| (8) perfume | s.a. | s.a. | s.a. | s.a. | s.a. | s.a. |
| (9) | | | | | | |

DETD As shown in Table C3 and Table C4, incorporation of xyloglucan, a thickening polysaccharide, and **sericin** has a synergistic effect, thus yielding an external-use composition having superior moisture retention and advantageous sensation in use.

DETD . . . propyleneglycol monostearate

1.5

| | |
|----------------------------------|-----------------|
| (9) POE (20) cetyl alcohol ether | 1.5 |
| (10) triethanolamine | 1.0 |
| (11) xyloglucan | 1.0 |
| (12) hydroxyethylcellulose | 1.0 |
| (13) sericin | 0.5 |
| (14) preservative | suitable amount |
| (15) antioxidant | suitable amount |
| (16) perfume | suitable amount |
| (17) purified water | balance |

DETD . . . 4.0

| | |
|-----------------------------------|-----------------|
| (9) POE (10) monooleic acid ester | 1.0 |
| (10) glyceryl monostearate | 1.0 |
| (11) xyloglucan | 2.0 |
| (12) xanthan gum | 0.1 |
| (13) sericin | 1.0 |
| (14) preservative | suitable amount |
| (15) colorant | suitable amount |
| (16) perfume | suitable amount |
| (17) purified water | balance |

DETD . . . 0.1

| | |
|---|-----|
| (6) polyoxyethylene sorbitan monostearate | 0.9 |
| (7) triethanolamine | 1.0 |
| (8) propylene glycol | 5.0 |
| (9) hydroxyethylcellulose | 0.5 |
| (10) xyloglucan | 0.5 |
| (11) sericin | 0.5 |
| (12) stearic acid | 2.2 |
| (13) isohexadecyl alcohol | 7.0 |
| (14) glyceryl monostearate | 2.0 |
| (15) liquid lanolin | 2.0 |
| (16) liquid paraffin. | |

CLM What is claimed is:

11. The external-use composition according to claim 6, further comprising **sericin**.

12. The external-use composition according to claim 11, wherein amounts of the xyloglucan, the thickening polysaccharide, and the **sericin** are as follows: (A) xyloglucan: 0.01-5.0% by weight with respect to the entirety of the external-use composition; (B) thickening polysaccharide: 0.01-5.0% by weight with respect to the entirety of the external-use composition; and (A) **sericin**: 0.001-5.0% by weight with respect to the entirety of the external-use composition.

L2 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2002 ACS
RN 193488-76-5 REGISTRY
CN **Sericin 1 (silkworm gene Ser1 isoform Ser1B precursor reduced)**
(9CI) (CA INDEX NAME)

OTHER NAMES:

CN GenBank Z48802-derived protein GI 755700
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2002 ACS
RN 164246-47-3 REGISTRY
CN **DNA (silkworm gene Ser1 sericin 1 isoform Ser1B cDNA plus flanks)**
(9CI) (CA INDEX NAME)

OTHER NAMES:

CN GenBank Z48802
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: AGRICOLA, CA, CAPLUS, GENBANK, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2002 ACS
RN 60650-89-7 REGISTRY
CN **Sericin B (9CI)** (CA INDEX NAME)
MF Unspecified
CI PMS, MAN
PCT Manual registration
LC STN Files: BIOBUSINESS, BIOSIS, CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2002 ACS
RN 60650-88-6 REGISTRY
CN **Sericin A (9CI)** (CA INDEX NAME)
MF Unspecified
CI PMS, MAN
PCT Manual registration
LC STN Files: AGRICOLA, CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2002 ACS

RN 37332-47-1 REGISTRY
CN Sericinase (9CI) (CA INDEX NAME)
MF Unspecified
CI MAN
LC STN Files: BIOSIS, CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)